REMARKS

I. Status

Claims 1-40 and 42-65 were pending. Claims 1-39 and 42-47 were withdrawn from consideration. Claims 40 and 48-65 were under examination. By virtue of this response, claims 40 and 48-65 have been have been cancelled without prejudice to future prosecution, and new claims 66 -72 have been added. ***[We can reduce excess claims fees by canceling additional claims]*** Accordingly, upon entry of this amendment, claims 66 -72 will be under consideration. Amendment and cancellation of certain of the claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented.

II. Interview

Applicants thank Examiner Kerr for the courtesy of a telephonic interview on July 27, 2004, with the undersigned and Dr. Gary Ashley. The participants discussed the allowabilty of the claims now presented as new claims 66-72.

III. Objections to the Specification

The specification is objected to because the title is allegedly not descriptive. Applicants are agreeable to amending the title, but propose doing so upon an indication of allowability of claims so that the new title is descriptive of those claims.

The Abstract was objected to as not completely describing the disclosed subject matter. The Abstract has been amended.

The amendment filed September 19, 2001, was objected to as introducing new matter (an incorporation by reference) in the paragraph captioned "Cross Reference to Related Applications." This paragraph has been amended.

The reference to "step 3b" in paragraph [371] was considered confusing by the Office. Paragraph [371] has been amended to remove this reference.

IV. The Objections and Rejections of Claims Articulated in the March 2004 Office Action

The objections and rejections of claims 40 and 48-65, as listed below, are moot in view of the cancellation of those claims. To the extent any of the previous rejections are believed relevant to new claims 66-72, Applicants have addressed them in Sections V and VI, below.

Claim 63 was objected to for a typographical error. (Office Action paragraph 10.[1])

Claims 49, 50, 52, 62, and 65 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. (Office Action paragraphs 11-14.)

Claims 40, 48-59, and 62-65 were rejected under 35 U.S.C. § 112, first paragraph, new matter, as allegedly failing to comply with the written description requirement. (Office Action paragraphs 15-16 and 20.)

Claims 52 and 64-65 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled in the specification. (Office Action paragraphs 17, 18 and 20.)

Claim 59 was rejected under 35 U.S.C. § 112, first paragraph, as allegedly requiring a deposit. (Office Action paragraph 19.)

Claims 40, 48, 49, 51, 55, 60, and 61 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Hofmann et al. (WO 99/42602) in view of Reichenbach et al., 1993, *Biotechnol. Adv.* 11:219-77,1993. (Office Action paragraph 21.)

V. New Claims

The new claims are supported in the specification are believed to add no new matter.

Claim 66 is directed to a method for isolating epothilone D from an epothilone D-producing *Myxococcus xanthus* cell by culturing the cell in the presence of XAD resin and methyl oleate. Comments by the Office in paragraph 18 of the Office Action are relevant to this claim.

Claims 67 and 68 depend from claim 66 and recite the further step of crystallizing epothilone D from a binary solvent system in which water is the forcing solvent. Support for a crystallization step in which epothilone D is crystallized from a binary solvent system in which water is the forcing solvent is found in the specification at, *e.g.*, paragraphs [364] and [373]-[374].

[1] References to the "Office Action" refer to the March 26, 2004Office Action .

The obviousness rejection articulated in paragraph 21 of the Office Action in connection with crystallization of epothilone at the end of purification," is discussed below in Section VI.

Claim 69 is directed to a method for obtaining epothilone D from an epothilone D-producing cell comprising culturing the cell in the presence of XAD resin; eluting the epothilone from the resin, subjecting the isolated epothilone D to further chromatography; and crystallizing the isolated epothilone D from a binary solvent system in which water is the forcing solvent, thereby obtaining epothilone D that is more than 95% purified. Claims 70-72 relate to obtaining epothilone D in crystalline form by crystallizing epothilone D from a binary solvent system in which water is the forcing solvent. As was discussed by the Examiner and Applicants' representative in the interview in July, although claim 70 does not include a step of culturing an epothilone producing cell, examination of claims 70-72 requires no additional search.

Claim 69 recites that epothilone D that is more than 95% purified is obtained. Support for purification to > 95% is found in the specification at, e.g., paragraphs [26], [374] and [380]. For clarity, Applicants note that the terms "purified" and "isolated" are described in the specification at paragraphs [58] and [59]. These terms, as used in the claims, do not indicate purification to homogeneity.

VI. The References Cited by the Office Do Not Render the Claimed Methods Obvious

Previously pending claims 40, 48, 49, 51, 55, 60, and 61 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Hofmann et al. (WO 99/42602) in view of Reichenbach et al., 1993, *Biotechnol. Adv.* 11:219-77,1993. Office Action paragraph 21. The Office stated that "Hoffmann et al. . . . teach crystallization of epothilone at the end of the purification."

As described in the accompanying declaration of Dr. Robert Arslanian, crystallization of epothilone D according to the claimed method was not described or suggested by Hoffmann. Hoffmann described crystallization of epothilone A and B but did not describe crystallization of epothilone D. Hoffman described crystallization using single- and double-solvent systems in which both solvents were organic but did not describe crystallization of epothilone D, or any epothilone, from a binary solvent system in which water is the forcing solvent. As described by Dr. Arslanian in the accompanying Declaration, the applicants were unable to obtain crystalline epothilone D using

methods described in Hoffman, but, surprisingly, were able to obtain epothilone D crystals using a binary system in which water was used as the forcing solvent. Without intending to be bound by a specific mechanism, this is likely because while crystalline forms of epothilone A and epothilone B are reportedly anhydrous, at least one form of crystalline epothilone D is a hemihydrate, a fact not described in the prior art. The advantage of using water as a forcing solvent for epothilone D crystallization was unexpected and was not suggested in the Hoffman reference.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

Dated: 9/27/04

Randolph Ted Apple
Reg. No. 36,429

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 650-326-2400
Fax: 415-576-0300
Attachments